Vancouver CoastalHealth

Dr Anna McGuire, Thoracic Surgeon
Vancouver General Hospital

September 30, 2025

To the Geoffrey Ogram Memorial Research Grant Review Committee
Lung Cancer Canada

Dear Members of the Adjudication Committee,

I am writing to express my intent to apply for the Geoffrey Ogram Memorial Research Grant in support of our project entitled *"Predicting Pathological Response Using CT-Based Radiomics in Non-Small Cell Lung Cancer (NSCLC) Patients Undergoing Neoadjuvant Chemo-Immunotherapy."*

This study addresses a pressing gap in lung cancer care: the inability of current imaging to accurately predict pathological response after chemo-immunotherapy. By applying advanced radiomics and machine learning to standard CT scans, we aim to non-invasively identify patients who may safely avoid unnecessary thoracotomies or benefit from tailored treatment escalation. Our multidisciplinary team—spanning thoracic surgery, radiology, pathology, and oncology—has already demonstrated feasibility through pilot data and is ideally positioned to execute this work across British Columbia's major thoracic centres.

This proposal aligns closely with the objectives of the GOMRG program:

- advancing **early detection methodologies** through innovative imaging biomarkers;
- improving understanding of lung cancer etiology in underrepresented groups, including non- and light smokers;
- and ensuring **direct clinical relevance for Canadians with lung cancer** by reducing morbidity and optimizing treatment pathways.

Although we have applied for CIHR Project Grant support to sustain long-term expansion, there remain critical gaps that require immediate funding—specifically, segmentation software acquisition, radiology/statistical consultation, and knowledge translation. The GOMRG's $25,000 contribution would be pivotal in ensuring these elements are realized and that our research findings can translate efficiently into clinical practice.

We respectfully submit this application and appreciate the opportunity to be considered for the Geoffrey Ogram Memorial Research Grant.

Sincerely,

Anna McGuire, MD, MSc (Clin Epidemiology), FRCSC
Associate Professor, Division of Thoracic Surgery
University of British Columbia / Vancouver General Hospital

Title: Predicting Pathological Response Using CT-Based Radiomics in NSCLC Patients Undergoing Neoadjuvant Chemo-Immunotherapy

1. BACKGROUND AND RATIONALE

Lung cancer remains the leading cause of cancer-related death in Canada, with non-small cell lung cancer (NSCLC) comprising approximately 85% of cases. Although advances in screening and systemic therapy have improved outcomes, survival remains poor, particularly for patients with resectable disease who do not achieve pathological response to neoadjuvant therapy.

Neoadjuvant chemo-immunotherapy (NCI) is now considered a standard of care for resectable NSCLC. However, clinicians currently lack reliable, non-invasive tools to assess response before surgery. CT and PET imaging are widely available but cannot consistently distinguish between viable tumor tissue and immune-mediated fibrosis or necrosis. Consequently, many patients undergo major thoracotomies even when their cancer has already been eradicated, while others who are unlikely to benefit are not identified early enough for alternative strategies.

Radiomics offers a novel solution by extracting hundreds of quantitative imaging features that reflect tumor heterogeneity, shape, and texture—patterns imperceptible to the human eye. By integrating radiomic features with clinical and pathological variables, artificial intelligence (AI) models can generate robust predictors of treatment response. Our team has piloted this approach in advanced NSCLC, demonstrating that radiomic signatures are associated with outcomes following immunotherapy. This proposal extends that work into the neoadjuvant setting, addressing a major gap in thoracic oncology.

2. RESEARCH OBJECTIVES

Hypothesis: Radiomic features from pre- and post-treatment CT scans, combined with clinicopathological variables, can accurately predict pathological complete response (pCR) and major pathological response (MPR) in patients treated with NCI.

Primary Objective:

- Identify radiomic features correlated with pCR and MPR in resectable NSCLC.

Secondary Objectives:

- Develop and validate machine learning (ML) models integrating radiomic, clinical, and pathological features.
- Explore delta-radiomics (changes in radiomic features from baseline to post-treatment) as predictors of pathological response.
- Assess generalizability of predictive models across institutions and subgroups, including sex, histology, and smoking status.
- Evaluate model interpretability using SHAP values and feature importance, ensuring clinical transparency.

3. METHODS

We will retrospectively study NSCLC patients (stage IB–IIIB) treated with NCI and surgical resection at four BC thoracic surgery centres (VGH, Surrey Memorial, Kelowna General, Royal Jubilee).

- **Patient Cohort:** Approximately 100 eligible patients treated between 2022–2025 with paired pre- and post-NCI CT scans and surgical pathology reports.
- **Radiomics Workflow:** Tumor segmentation using semi-automated software (MINT Lesion™), feature extraction with PyRadiomics, and harmonization according to IBSI standards. Both static and delta-radiomics features will be derived.
- **Model Development:** Multiple ML classifiers (Random Forest, SVM, XGBoost, CatBoost) trained using nested cross-validation, optimized for AUC performance. Class imbalance will be mitigated using stratified resampling.
- **Validation:** Internal validation using 30% held-out data, plus external validation across centres. Models will be benchmarked against clinical predictors alone to assess added value of radiomics.
- **Equity and SGBA+:** Sex as a biological variable will be included in all analyses. Subgroup modeling will be performed for never-smokers and light ex-smokers, historically excluded from lung cancer screening studies.

4. EXPECTED OUTCOMES

We anticipate producing a validated, non-invasive radiomics model capable of predicting pCR and MPR with strong discriminative accuracy (AUC >0.80). This will:

- Enable more precise surgical decision-making by identifying patients likely to have achieved complete response.
- Reduce morbidity by sparing some patients from unnecessary thoracotomy and associated complications.
- Allow timely escalation of therapy in non-responders, potentially improving survival.
- Provide pilot evidence to launch a prospective, pan-Canadian validation trial.
- Generate open-access datasets and standardized pipelines to accelerate further radiomics research in lung cancer.

5. RELEVANCE TO GOMRG PRIORITIES

This research directly fulfills the mandate of the Geoffrey Ogram Memorial Research Grant:

1. **Early Detection:** Radiomics offers a non-invasive imaging biomarker for identifying treatment response before surgery.
2. **Etiology Across Demographics:** Our analyses explicitly include non-smokers and light ex-smokers, groups underrepresented in current screening guidelines but increasingly recognized in Canadian lung cancer epidemiology.
3. **Direct Impact on Canadian Patients:** By reducing unnecessary surgeries, improving treatment selection, and enabling precision oncology, this project has immediate translational benefit and the potential to reduce lung cancer burden nationwide.

6. APPENDIX

Preliminary Data

DATA 1. Comparison between two groups with different pathological response

Clinical and Imaging Parameters	pCR or MPR	Non- pCR/MPR
Female: Male	1:2	5:2
Smoker: Non-Smoker	2:1	7:0
cTNM stage (8th Edition)	Ib:1; III:3	II:3; III:4
Lung Tumor		
Nodule type (Solid: Part Solid)	3:0	6:1
Histological Type (Adeno: Others)	3:0	5:2
Location: (Central vs Non-central)	2:1	4:3
On pre-NCI CT:		
Diameter, in mm	30.2±13.3	44.0±14.3
Density, in HU	-70.56±157.2	-29.9±131.6
On post-NCI & pre-surgical CT:		
Diameter, in mm	16.3±5.6	44.3±14.7 *
Density, in HU	-89.2±182.4	-10.6±92.8
Δ Size (Pre-Post), in mm	13.8±9.7	-0.2±8.5 *
Δ Density (Pre-Post), in HU	18.6±25.1	-19.2±57.6
On Pre-NCI PETCT: tumor SUV_{max}	19.1±13.8	11.1±4.2

*: p<0.05

DATA 2. ROC result shows Δ radiomics signature from lung tumor using both pre- and post-NCI CT scan can predict good pathological response (i.e., pCR/MPR)

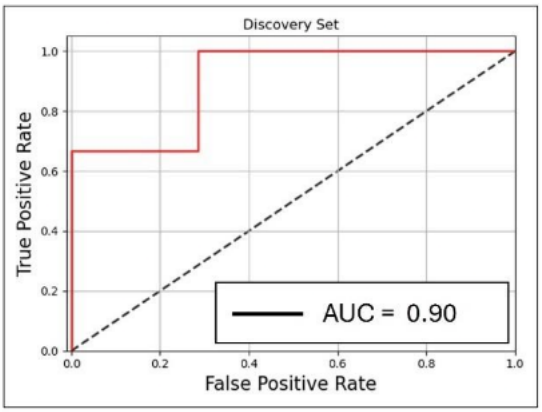

Figure 1: Comparison between two groups with different pathological response and ROC result shows A radiomics signature from lung tumor

Timeline

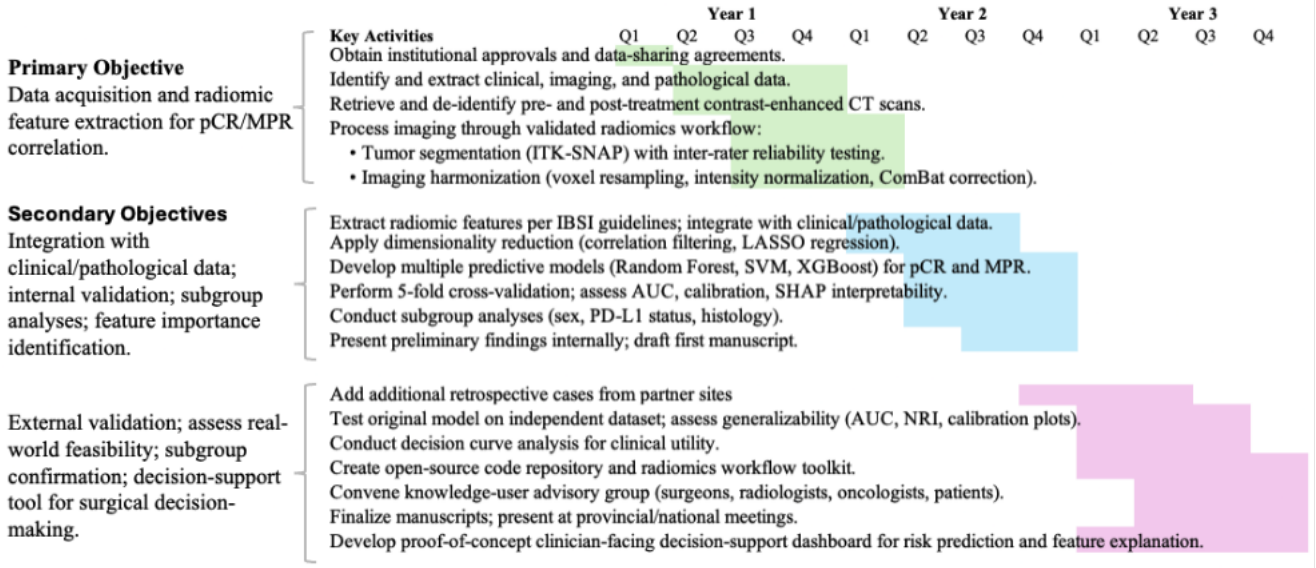

Figure 2: GANTT Chart of Project Objectives and Activities

IMPACT STATEMENT

This project will exert a **sustained, field-shaping influence** by advancing radiomics as a validated biomarker for treatment response in resectable non-small cell lung cancer (NSCLC). Current imaging modalities (CT, PET) cannot reliably predict which patients have achieved pathological complete response (pCR) or major pathological response (MPR) after neoadjuvant chemo-immunotherapy (NCI). As a result, many patients undergo unnecessary thoracotomies while others are not escalated to alternative therapies in time.

By integrating **quantitative CT radiomics features** with clinical and pathological variables, our team will deliver a reproducible, non-invasive predictive model that can be implemented in routine radiology workflows. This approach is cost-effective, scalable, and readily applicable across Canadian cancer centres.

Influence on the research field:

- Establishes radiomics as a translational imaging biomarker in lung cancer, accelerating AI adoption in thoracic oncology.
- Provides a standardized pipeline for imaging harmonization and machine learning interpretability, creating a foundation for multi-centre collaboration.
- Supplies pilot data and proof of feasibility for a prospective pan-Canadian validation trial.

Impact on patients and healthcare:

- **Reduced mortality:** Earlier escalation of therapy in predicted non-responders will lower recurrence rates and improve survival.
- **Reduced morbidity and improved quality of life:** Avoiding unnecessary thoracotomy spares patients pain, complications, and long recoveries.
- **Optimized care:** Stratification of responders and non-responders ensures treatment is personalized, efficient, and evidence-based.
- **Reduced burden on the system:** Fewer operations translate to significant healthcare savings and improved allocation of surgical resources.

In the **short to medium term**, this project will accelerate knowledge translation from radiomics science into clinical practice, producing a predictive tool that directly reduces the burden of lung cancer and improves outcomes for Canadians.

PUBLIC, NON-SCIENTIFIC SUMMARY

Title: *Using Artificial Intelligence and CT Scans to Improve Lung Cancer Treatment*

Lung cancer is the leading cause of cancer death in Canada. For many patients, doctors now use a combination of chemotherapy and immunotherapy before surgery to shrink or even eliminate tumors. This approach, called *neoadjuvant chemo-immunotherapy*, has helped improve outcomes. But there is a major problem: today's imaging tests, like CT or PET scans, cannot clearly show whether the cancer has been completely destroyed.

Because of this, most patients still undergo major lung surgery even if the cancer may already be gone. Lung surgery is serious — it can cause pain, complications, and long recovery times. At the same time, some patients who have not responded to treatment are not identified early enough to receive different therapies that could help them.

Our project offers a new solution. We are using a method called **radiomics**, which applies advanced computer analysis and artificial intelligence (AI) to routine CT scans. Radiomics extracts hundreds of hidden features from images, capturing subtle patterns that human eyes cannot see. By combining these imaging features with other patient information — such as age, smoking history, and pathology results — we will build a computer model that can predict whether a patient has fully responded to treatment.

Why is this important?

- **Better care for patients:** Those who have no cancer left may be able to avoid unnecessary surgery.
- **Improved quality of life:** Patients who skip major surgery can recover faster, with less pain and fewer risks.
- **More effective treatment:** Patients predicted not to have responded can be offered different therapies sooner, improving their chances of survival.
- **Smarter healthcare:** By avoiding surgeries that are not needed, we save hospital resources and reduce the burden on the healthcare system.

Our team brings together surgeons, radiologists, oncologists, and pathologists from across British Columbia. We have already shown in smaller studies that radiomics can successfully predict how advanced lung cancers respond to treatment. This grant will allow us to expand this approach to patients receiving chemo-immunotherapy before surgery — a growing group in Canadian cancer care.

In the future, this research could lead to a new tool in every hospital: an AI-based system that analyzes CT scans and tells doctors which patients still need surgery and which may already be cured. For Canadians, this means more personalized treatment, fewer unnecessary operations, and better survival.

BUDGET

Personnel – $10,000

- **Radiologist (MD, fellowship-trained, >10 years experience):** Independent review of CT scans, segmentation quality assurance.
- **Statistician (MSc level, >5 years experience):** Model training, validation, interpretability analysis.
  Justification: Expert time is essential for accurate radiomics feature validation and robust machine learning analysis. These roles are not covered in CIHR funding.

Software and Equipment – $10,000

- **Semi-automated segmentation software license (MINT Lesion™ lung module).**
  Justification: Reduces manual workload, standardizes feature extraction, and ensures reproducibility across multi-site datasets.

Knowledge Translation – $5,000

- **Open-access publication fees** and **knowledge translation activities** (dissemination workshops with clinicians, creation of lay summaries for patient groups).
  Justification: Ensures rapid and equitable access to results, directly supporting GOMRG's mandate to accelerate translation into optimized patient care.

Other Funding Sources:

- We have applied for a CIHR Project Grant ($670,000, pending) to support broader infrastructure and long-term expansion.
- The requested $25,000 from GOMRG covers **immediate gaps** (software, personnel time, KT) that are not duplicated or funded elsewhere.

INVESTIGATOR TEAM

Principal Investigator (PI):

- Dr. Anna McGuire, MD, MSc (Clin Epidemiology), FRCSC – Thoracic Surgery, UBC / Vancouver General Hospital

Co-Principal Investigator (Co-PI):

- Dr. Ren Yuan, MD – Radiology, BC Cancer

Co-Investigators (Co-Is):

- Dr. Julia Naso, MD, PhD – Pathology, UBC
- Dr. Cheryl Ho, MD – Medical Oncology, BC Cancer

CCVs Provided:

- Dr. Anna McGuire (PI)
- Dr. Ren Yuan (Co-PI)

THE UNIVERSITY OF BRITISH COLUMBIA

Ahmer Karimuddin MD, FRCSC
Professor
C.N. Woodward Chair in Surgery
Head, Department of Surgery
Diamond Health Care Centre
11th Floor - 2775 Laurel Street
Vancouver, B.C. Canada V5Z 1M9
surgery.med.ubc.ca

September 29, 2025

To the Geoffrey Ogram Memorial Research Grant Review Committee,

I am writing to express our strongest support for the application entitled *"Predicting Pathological Response Using CT-Based Radiomics in Non-Small Cell Lung Cancer (NSCLC) Patients Undergoing Neoadjuvant Chemo-Immunotherapy"* submitted by Dr. Anna McGuire and colleagues. We are proud to endorse this innovative project, which aims to leverage advanced radiomic analysis of thoracic imaging to improve prediction of treatment response and outcomes in lung cancer.

This research directly aligns with the mission of the Geoffrey Ogram Memorial Research Grant to foster impactful, patient-centered lung cancer research. Radiomics offers a unique opportunity to extract high-dimensional, quantitative features from standard-of-care imaging, enabling non-invasive characterization of tumor biology. Such approaches hold promise to improve clinical decision-making, personalize treatment selection, and ultimately enhance patient outcomes.

I confirm that the proposed research is feasible at our institution, which provides the necessary archives, computational resources, and multidisciplinary expertise to support the successful completion of the project. Our institution is committed to providing the infrastructure and oversight required to ensure its success.

Ahmer Karimuddin MD, FRCSC
Professor and C.N. Woodward Chair in Surgery
Head, Department of Surgery
The University of British Columbia